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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,937	07/31/2001	Charles Joel Arntzen	P00245USF	4815

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 10/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,937	ARNTZEN ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-87* is/are pending in the application.

4a) Of the above claim(s) *1-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0701*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group IX, claims 73-76 and 78-87 in the reply filed on July 7, 2004 is acknowledged. The traversal is on the ground(s) that the restriction between inventions IX and X (claim 77) is improper. Upon further consideration, the restriction requirement between inventions IX and X is withdrawn, and claims 73-87 are examined on the merits.

The requirement is still deemed proper with respect to inventions I-VIII and is therefore made FINAL. Claims 1-72 are withdrawn from consideration as being directed to nonelected inventions.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed July 31, 2001, is attached to the instant Office action.

Priority

This application lacks the necessary references to the prior applications. The current reference to prior applicants is incomplete. A statement reciting the prior applications to which this application claims priority should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of the parent nonprovisional application(s) should be included.

Claim Objections

Claims 76 and 86 are objected to because of the following informalities: the claims recite the acronym "TGEV" without reciting what the acronym designates. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a vector for transforming a plant, including a plasmid or viral vector and including a vector capable of achieving expression levels of 0.1%, 0.05%, or 0.03% total soluble protein, said vector comprising: a DNA sequence encoding a recombinant viral antigen protein, including a protein from TGEV and including a truncated viral antigen protein, said protein being antigenic to an animal and including a protein that is chimeric by being fused to another peptide, polypeptide or protein such that expression of the protein is enhanced; and a plant functional promoter operably linked to said DNA sequence which directs the expression of said protein in said plant, including a DNA sequence wherein expression of the recombinant viral antigen protein is

preferentially directed to the seed of said plant and including a promoter that preferentially expresses the viral antigen protein in an edible portion of the plant, and including a plasmid vector further comprising a translational enhancing sequence.

The specification describes four plasmid vectors for transforming a plant, pHVA-1, pHB101, pHB102 and pPS-TG. The specification describes plasmid vectors pHVA-1 and pHB101 as comprising a DNA sequence encoding a Hepatitis B surface antigen (HbsAg) protein and a plant functional cauliflower mosaic virus (CaMV) 35 S promoter sequence operably linked thereto (page 21; Figures 1 and 2; page 25; Figures 3 and 5). The specification also describes pHB101 as achieving expression levels of 3 to 10 ng/mg soluble protein in transgenic tobacco leaves (page 29; Figure 6B). The specification describes plasmid vector pHB102 as comprising a DNA sequence encoding a Hepatitis B surface antigen (HbsAg) protein and a plant functional modified CaMV 35 S promoter sequence which contains a duplication of the upstream regulatory sequences between nucleotides –340 and –90 relative to the transcription start site and which has fused at its 3' end the tobacco etch virus 5' nontranslated leader sequence which acts as a translational enhancer in tobacco cells, operably linked thereto (pages 25-26; Figure 4). The specification also describes pHB102 as achieving expression levels of 25-65 ng/mg soluble protein in transgenic tobacco leaves, 70 ng/mg soluble protein in transgenic tomato leaves, and 43 ng/mg soluble protein in transgenic red tomato fruit (page 29; Figure 6B; page 32). The specification describes plasmid vector pPS-TG comprising a DNA sequence encoding a Transmissable Gastroenteritis Virus (TEGV) S-protein that is truncated at the 5' end six base pairs upstream of the translation initiation site and a plant

functional patatin promoter sequence operably linked thereto which drives tuber-specific expression in potato plants (page 34).

The specification does not describe viral vectors, or vectors that achieve other levels of expression such as the levels recited in the rejected claims, or vectors comprising DNA sequences encoding recombinant viral antigen proteins other than the Hepatitis B surface antigen (HbsAg) protein and the Transmissable Gastroenteritis Virus (TEGV) S-protein, or vectors comprising truncated viral antigen proteins other than the truncated Transmissable Gastroenteritis Virus (TEGV) S-protein, or vectors comprising a viral antigen protein that is chimeric by being fused to another peptide, polypeptide or protein such that expression of the protein is enhanced, or vectors comprising promoters that that preferentially express the viral antigen protein in seed or in an edible portion of the plant other than a potato tuber, or vectors comprising translational enhancing sequence other than the tobacco etch virus 5' nontranslated leader sequence.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus which encompass vectors comprising DNA sequences encoding any and all recombinant viral antigen proteins obtained from any and

all sources and their truncations, and that further comprise any and all peptides, polypeptides and proteins that enhance protein expression and that further comprise promoters that that preferentially express the viral antigen protein in seed or in any and all edible portions of any and all plants and that further comprise any and all translational enhancing sequences. Applicant also has not described the structural features unique to the genus that are correlated with the claimed levels of expression and expression modifying functions.

Claims 79-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a vector for transforming a plant said vector being capable of achieving expression levels of 0.1%, 0.05%, or 0.03% total soluble protein and said vector comprising: a DNA sequence encoding a recombinant viral antigen protein, said protein being antigenic to an animal; and a plant functional promoter operably linked to said DNA sequence which directs the expression of said protein in said plant, including a vector

The specification discloses how to make and use four plasmid vectors for transforming a plant, pHVA-1, pHB101, pHB102 and pPS-TG. The specification discloses plasmid vectors pHVA-1 and pHB101 as comprising a DNA sequence encoding a Hepatitis B surface antigen (HbsAg) protein and a plant functional

cauliflower mosaic virus (CaMV) 35 S promoter sequence operably linked thereto (page 21; Figures 1 and 2; page 25; Figures 3 and 5). The specification also discloses pHB101 as achieving expression levels of 3 to 10 ng/mg soluble protein in transgenic tobacco leaves (page 29; Figure 6B). The specification discloses plasmid vector pHB102 as comprising a DNA sequence encoding a Hepatitis B surface antigen (HbsAg) protein and a plant functional modified CaMV 35 S promoter sequence which contains a duplication of the upstream regulatory sequences between nucleotides –340 and –90 relative to the transcription start site and which has fused at its 3' end the tobacco etch virus 5' nontranslated leader sequence which acts as a translational enhancer in tobacco cells, operably linked thereto (pages 25-26; Figure 4). The specification also discloses pHB102 as achieving expression levels of 25-65 ng/mg soluble protein in transgenic tobacco leaves, 70 ng/mg soluble protein in transgenic tomato leaves, and 43 ng/mg soluble protein in transgenic red tomato fruit (page 29; Figure 6B; page 32). The specification discloses plasmid vector pPS-TG comprising a DNA sequence encoding a Transmissable Gastroenteritis Virus (TEGV) S-protein that is truncated at the 5' end six base pairs upstream of the translation initiation site and a plant functional patatin promoter sequence operably linked thereto which drives tuber-specific expression in potato plants (page 34).

The specification does not disclose how to make and use vectors that achieve other levels of expression, such as the expression levels recited in the rejected claims.

The claimed invention is not enabled because expressing a recombinant protein at specific levels in transgenic plants is unpredictable. Expressing a recombinant protein at the specific levels in transgenic plants is unpredictable because the level of expression is

affected by multiple variables, variables which include but are not limited to the type of promoter and terminator used in the expression vector, the plant species transformed by the expression vector, the type of tissue in which the protein is expressed, the stability of the mRNA transcribed from the recombinant protein coding sequence, the translation efficiency of the mRNA transcribed from the recombinant protein coding sequence, and the stability of the recombinant protein. Accordingly, different levels of expression would be expected for different types of recombinant proteins, or for the same protein expressed from different types of expression vectors, or for the same protein expressed in different species or in different tissues.

See, for example, Sanders et al. (Nucleic Acids Research, 1987, Vol. 15, No. 4, pages 1543-1558), who teach that NPTII mRNA transcript levels were 30 fold higher in plants transformed with vectors comprising a DNA sequence encoding NPT II operably linked to a CaMV 35S promoter and leader sequence as compared to plants transformed with vectors comprising a DNA sequence encoding NPT II operably linked to a nopaline synthase promoter and leader sequence (page 1543 abstract; page 1552 figure 3 ; page 1553 table 1; page 1552 figure 4).

See also, for example, Schouten et al. (Plant Molecular Biology, 1996, Vol. 30, pages 781-793), who teach that expression levels of a single-chain antibody reached up to 0.2% of total soluble protein in tobacco plants transformed with vectors comprising a DNA sequence encoding the single-chain antibody fused to a C-terminal KDEL endoplasmic reticulum retention signal peptide, as compared to undetectable protein expression levels in tobacco plants transformed with vectors comprising a DNA sequence encoding the single-chain antibody lacking the KDEL sequence (page 781 abstract; page

787 Figure 3; page 788 Figures 4 and 5; page 789 Figure 6). Schouten et al. also teach that the differences in protein expression levels could not be explained by differences in expression levels of the mRNAs (page 781 abstract; page 788 Figure 5).

In the instant case the specification does not provide sufficient guidance for one skilled in the art to express at the claimed levels, without undue experimentation, any and all recombinant viral antigen proteins, as the specification does not disclose expression at the claimed levels of any recombinant viral antigen protein. Absent sufficient guidance with respect to which type vector construct to use with which type of recombinant viral antigen protein to achieve the claimed level of expression, one skilled in the art would have to test the expression level of each and every recombinant viral antigen protein expressed from each and every type of plant transformation vector in a variety of different plant types and tissues order to discriminate between those plant transformation vectors that would express a recombinant viral antigen protein at the claimed level and those that would not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 77 is indefinite in the recitation of "said protein being antigenic to a human or an animal". It is unclear how an antigen would be antigenic to a human or an animal, as a human is an animal.

Claims 79, 80 and 81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 79, 80 and 81are indefinite in the recitation of "capable of". It is unclear whether the actual achievement of the recited expression levels is necessary to practice the claimed invention.

Claims 82, 83, 84 and 85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 82, 8,3 84 and 85 are indefinite in the recitation of "the plasmid vector of claim 73". There is insufficient antecedent basis in claim 73 for this limitation, as claim 73 is not directed to a plasmid vector.

Claim 85 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 85 is indefinite in the recitation of "an edible portion". It is unclear what portion of the plant is being referred to, as different portions of different plants are edible with respect to different types of organisms that eat plants.

Claim 87 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 87 is indefinite in the recitation of "wherein said vector directs expression". There is insufficient antecedent basis in claim 73 for this limitation, as claim 73 recites that the promoter of the vector directs expression.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 73, 74 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Jabbar et al. (Proc. Natl. Acad. Sci. USA, April 1985, Vol. 8, pages 2019-2023).

The claims are drawn to a plasmid vector for transforming a plant, said vector comprising: a DNA sequence encoding a recombinant viral antigen protein, said protein being antigenic to a human or an animal and a plant functional promoter operably linked to said DNA sequence which directs the expression of said protein in said plant.

Jabbar et al. teach a plasmid vector comprising: a DNA sequence encoding a recombinant Influenza viral antigen protein, said protein being antigenic to a human or an animal and a yeast functional promoter operably linked to said DNA sequence which directs the expression of said protein in said yeast (page 2020 Figure 1). While Jabbar et al. do not teach that their plasmid vector is "for transforming a plant", they need not teach such a use, as the recitation of "for transforming a plant" in the preamble of the claim is an intended use for the claimed vector and as such does not limit the claimed vector. Further, while Jabbar et al. do not teach that the yeast functional promoter is also a plant functional promoter, the yeast functional promoter is presumed to function in a plant cell, or in any other type of eukaryotic cell, because the eukaryotic transcriptional machinery is conserved across the eukaryotic kingdoms.

Claims 73, 75 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Schmaljohn et al. (Journal of Virology, July 1990, Vol. 64, No.7, pages 3162-3170).

The claims are drawn to a viral vector for transforming a plant, said vector comprising: a DNA sequence encoding a recombinant viral antigen protein, said protein being antigenic to a human or an animal and a plant functional promoter operably linked to said DNA sequence which directs the expression of said protein in said plant.

Schmaljohn et al. teach Baculovirus and Vaccinia Virus viral vectors comprising: a DNA sequence encoding a recombinant Hantaan viral antigen protein, said protein being antigenic to a human or an animal and an insect or mammalian cell functional promoter operably linked to said DNA sequence which directs the expression of said protein in said insect or mammalian cells (page 3165 Figure 1). While Schmaljohn et al. do not teach that their viral vector is "for transforming a plant", they need not teach such a use, as the recitation of "for transforming a plant" in the preamble of the claim is an intended use for the claimed vector and as such does not limit the claimed vector. Further, while Schmaljohn et al. do not teach that the insect or mammalian cell functional promoter is also a plant functional promoter, the insect or mammalian cell functional promoter is presumed to function in a plant cell, or in any other type of eukaryotic cell, because the eukaryotic transcriptional machinery is conserved across the eukaryotic kingdoms.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 73-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-7 of U.S. Patent No. 6,034,298. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed vectors for transforming a plant that comprise a DNA sequence encoding a recombinant viral antigen protein and a plant functional promoter operably linked to said DNA sequence are obvious variants of the plasmid vectors for transforming a plant comprising a DNA sequence encoding a recombinant viral antigenic protein claimed in the patent.

Claims 73-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,484,719. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed vectors for transforming a plant that comprise a DNA sequence encoding a recombinant viral antigen protein and a plant functional promoter operably linked to said DNA sequence are obvious variants of the plasmid vectors comprising a DNA sequence encoding a recombinant hepatitis B viral surface antigen protein claimed in the patent.

Claims 73-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 and 18-36 of U.S. Patent No. 6,551,820. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed vectors for transforming a plant that comprise a DNA sequence encoding a recombinant viral antigen protein and a plant functional promoter operably linked to said DNA sequence are obvious variants of the plant expression vectors and polynucleotides that comprise polynucleotides encoding viral antigen polypeptides claimed in the patent.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins Cynthia Collins 9/30/04